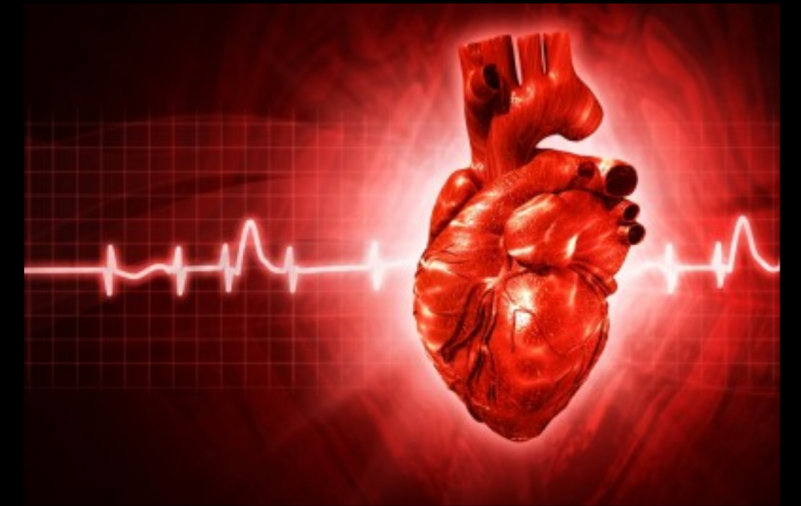
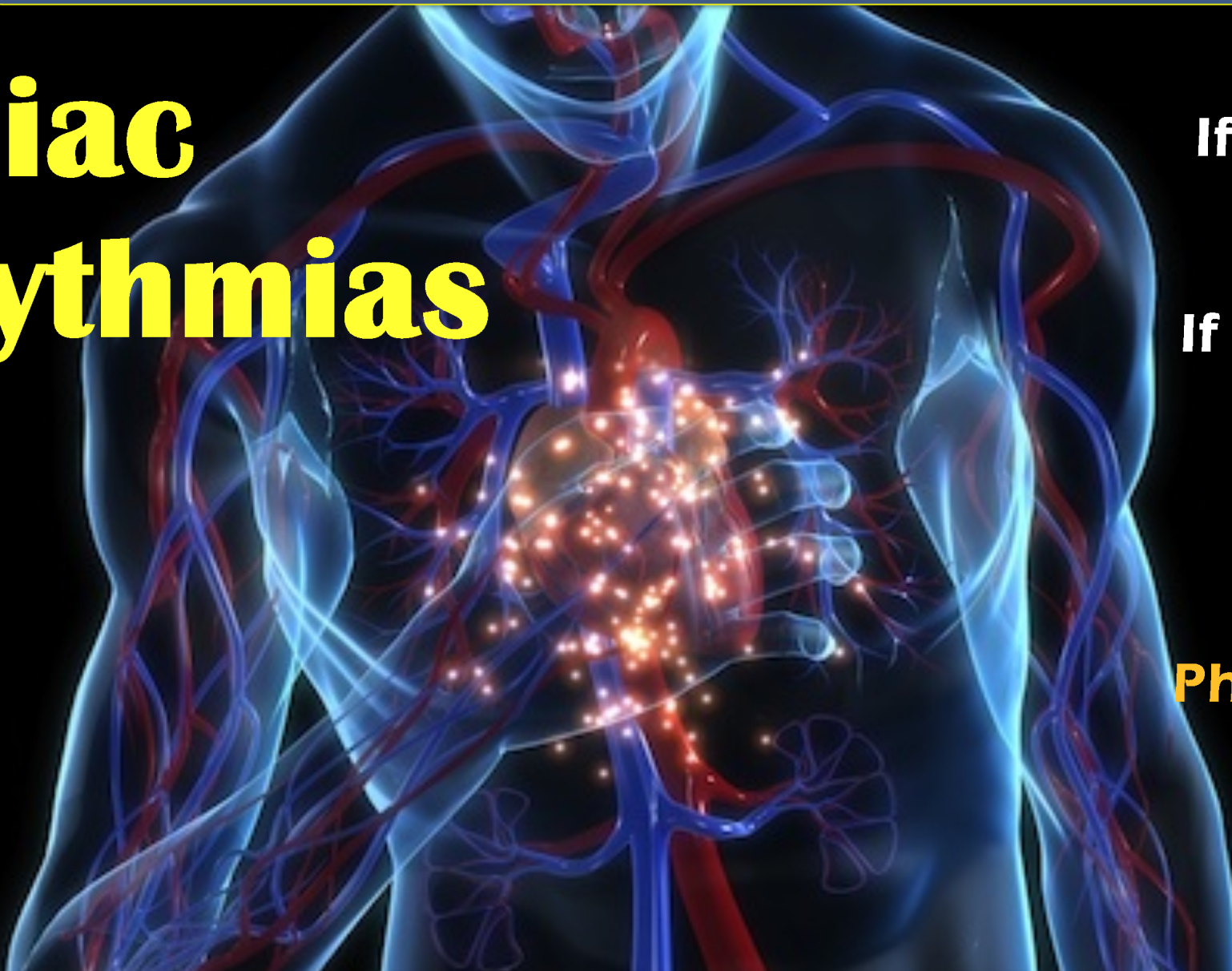


Draw Pharmacology *in your mind*



Cardiac arrhythmias



If you are a pharmacy student
If you are postgraduate and want
to revise pharmacology by an
easy way
If you are using any pharmacology
reference
this file will aid you
> And wait for more <

Follow me at
Pharmacistalaanasr.wordpress.com

Contact me at
Pharm.alaa@gmail.com

لا تنسوني من صالح دعائكم

Pharmacist. **Alaa Nasr**

د. آلاء نصر

VISIT...

LANZAROTE
Caliente.COM

CARDIAC ARRHYTHMIAS

- Arrhythmia is a disease characterized by:

→ ↑ in heart rate → **Tachyarrhythmia**
 → ↓ in heart rate → **Bradyarrhythmia**

Types

1. Sinus arrhythmias

- It is **not pathological** → **Tachyarrhythmia**
- Common in **young healthy people**
- **Causes**
- Fever - Anemia - Excitement situations (*fight, fright, flight, happiness, sadness*) - Hyperthyroidism (↑ levels of T_3 and T_4) - Sympathomimetic drugs

2. Atrial flutter

- It results from a **diseased heart** → **Pathological** (ex. *Rheumatic fever - Myocarditis*)
- The atria beat very rapidly but **regularly** (coordinated)
- **Atrial rate = 300 beat/min**
- Not all these beats cause ventricular contraction 1/2 this number are delivered to ventricles
- **Ventricular rate = 150 beat/min**

Etiology
Ectopic focus → the heart will consider it as the new pacemaker (it is a specific tissue in the heart that takes over the function of SAN because it has a **higher** beating rate than SAN, it beats regularly)

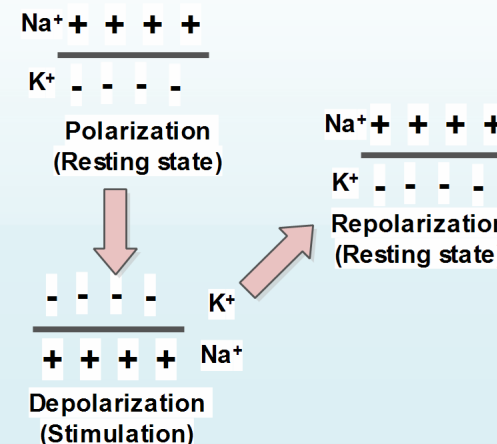
3. Atrial fibrillation

- **Atrial rate = 500 beat/min**
- **Ventricular rate = 80-100 beat/min**
- ONLY 1/5 of atrial beats are delivered to ventricles **WHY!!**
- As these 500 beats are not real, not strong beats but they are → **irregular, very rapid, uncoordinated & fragmentary** → so, they can be called **muscle twitches**, palpitations, fibrillations → **mechanically ineffective to pump blood** → **most of them do not survive to reach AVN and AV bundle**
- As the atrial rate is **not regular** → the ventricular systole will be **irregular** and of variable strength

➔ **Atrial flutter is more dangerous than atrial fibrillation** → as it may cause "ventricular fibrillation" → can lead to **congestive heart failure (CHF)**

Useful tips for understanding mechanisms .. Remember

- There is a **potential difference** across the plasma membrane of each cell where
 → **+ve charge accumulate outside the membrane**
 → **-ve charge accumulate inside the membrane**
- Any mechanical change in the muscle is preceded by electrical change (*electrical stimulus, depolarization*)



- In the heart the electrical change is initiated by an electrical stimulus from **SAN** or other electrical stimulus (**Ectopic focus**) → this electrical change is due to movement of ions → **each type of ions has its specific type of channels**:
 → **Na^+ channels** → blocked by tetrodotoxin
 → **Ca^{+2} channels** → blocked by Nifedipine, Verapamil .. etc (calcium channel blockers CCBs)
- Ca^{+2} is present in the **sarcoplasmic reticulum** → it is released after depolarization to be free in the muscle fiber → helps in joining **actin and myosin** → leading to contraction
- The energy for muscle contraction is obtained from → hydrolysis of ATP by ATPase present in the muscle fibrils

- They slow the depolarization process (↑ refractory period) .. **How !**
- They cause **partial occlusion of Na^+ channels** → so, a **higher concentration gradient** should be established outside the membrane in order to cause excitation to the membrane
- So, rate of depolarization will ↓ → and also outflux of Na^+ will be hindered → rate of repolarization will ↓
- So, there will be **prolongation of depolarization-repolarization cycle**
- So, refractory period will ↑ and speed of conduction will ↓
 → Heart rate will be slowed down
- They are **membrane stabilizers** (have the ability to stabilize the membrane) = ↓ its excitability = ↑ threshold of excitation
- They are classified into **3 subclasses** according to their **affinity to Na^+ channels**

1. Cardiac actions

- It has **2 actions that seem to be opposite !!**
- 1. **Depressant** effect on cardiac muscle
- 2. **Atropine-like** action (antivagal action, parasympatholytic)
- So, let's figure out are these 2 effects **parallel or opposite**

Effect on heart rate

In normal heart

- Here, **SAN** is the pacemaker of the heart → it is the least sensitive part in the heart to the depressant effect of Quinidine → **it receives vagal supply** (inhibitory effect on the heart)
- So, here Quinidine has both effects:
 1. **Depressant effect** → little effect on SAN
 2. **Atropine-like action** → inhibition on vagal action SAN → stimulation
 → **Opposite actions**
 → Net effect → **↑ heart rate**

In arrhythmic heart

- Here, the **Ectopic focus** is the pacemaker of the heart → it **does not receive vagal supply** (not controlled by vagus nerve)
- So, the **depressant action of Quinidine predominates** (no antivagal action) → **↓ heart rate**

Effect on refractory period

- **Depressant action** → ↑ refractory period
- **Atropine-like action** → ↓ refractory period (vagal stimulation ↓ refractory period)
 → So these are **parallel actions**

Effect on conduction velocity

- **Depressant action** → ----
- **Atropine-like action** → you should now that vagal stimulation ↓ conductivity of the AV bundle → so, number of impulses transmitted from atria to ventricles ↓
 → Quinidine has **antivagal action** → ↑ conductivity of AV bundle → so, ↓ atrial rate but ↑ ventricular rate (↑ velocity of conduction of AVN and AV bundle) → so, may lead to **ventricular fibrillation**

2. Other actions

Effect on ECG

Prolongs PR interval, QRS complex, QT interval

➔ So, regimen of **Digitalis and Quinidine** should be used for patients who have:
 1. Recently developed atrial arrhythmia
 2. Little or no impairment of ventricular arrhythmia
Why !
 As digitalis ↓ the speed of conduction in AVN and AV bundle (Extravagal mechanism)
 → **Quinidine** for atria & **Digitalis** for ventricles

Antiarrhythmics

Mechanism

1. Class I

1) Class Ia

Quinidine

α-blocking action

- Cause **vasodilatation** → **hypotension** → leading to activation of **compensatory mechanisms** →
 1. Reflex tachycardia !
 2. Reflex stimulation of sympathetic nervous system !
 → Dangerous side effects → may **oppose** the main use !!

Curare-like action

Neuromuscular blocking effect

They are Ca^{+2} channel blockers → interfering with the entry of Ca^{+2} → so, ↓ force of contraction

ex.
Verapamil (Cardiomil® - Isoptin®)
Diltiazem (Delay-tiazem® - Altiazem®)
Cinnarazine (Stugeron® - Cinibral®)
Nifedipine (Epilat® - Adalat®)
Nicardipine (Pelcard®)

4. Class IV



They prolong the refractory period of cardiac muscle by other mechanisms
ex. Amiodarone (Cordarone®)

3. Class III

Antiarrhythmics

Ph. Alaa Nasr

1. Example

β-blocker → **Propranolol** (Inderal®)

2. Mechanism

- **Sympatholytics** → so, antagonizing the sympathetic effect on the heart
- Propranolol has a **Quinidine-like action**

3. Uses

Used as a **preanesthetic medication** before some general anesthetics such as **Halothane**
Notice that .. Halothane ↑ the sensitivity of SAN to endogenous catecholamines → ↑ heart rate

2. Class II

4. Disadvantages

High doses can lead to **heart failure** → as they deprive the heart from sympathetic influence causing bradycardia then HF

Solution

1. Use β-blocker with ISA (*intrinsic sympathomimetic activity*) → partial agonist → **ex. Pindolol**
2. Coadministration with **Atropine** → ↓ bradycardia (*blocks the inhibitory effect of parasympathetic nerve*)

May lead to **Asthma** → due to non-selectivity → it may block β_2 receptors in lungs → bronchoconstriction

Solution

Use a selective β_1 blocker → **ex. Atenolol**

1. Atrial flutter
2. Atrial fibrillation
3. Paroxysmal atrial tachycardia
4. Paroxysmal ventricular tachycardia

3. Uses

1. Administered orally as Quinidine sulphate
2. Rapidly absorbed - Hepatic metabolism - Excreted in urine (20% as it is)
3. Peak concentration in the plasma is attained in 60-90 min
4. **70-80% plasma protein binding** → can be displaced by **Digitalis** → **TOXICITY**

4. Kinetics

5. Side effects & Toxicity

1. **GIT** → Nausea - Vomiting - Diarrhea
2. **CVS**:
 - **Severe depression** → may cause heart failure in toxic doses
 - **Hypotension** → due to α -blocking action
 - **Tachycardia** → due to **Atropine-like** & α -blocking actions
 - Complains of **muscle weakness** → due to **curare-like** action

Quinidine

1) Class Ia

1. Class I

Procainamide

- It has a pharmacological action **similar to Procain** (a local anesthetic) but it is "**amide**" so,
 1. It is not readily metabolized by plasma esterase → ↑ the duration of action
 2. Effective orally
 • Its **cardiac actions** are identical to those of **Quinidine**
 • It can be administered **orally - IV - IM**

2) Class Ib

Phenytoin

- Anti-epileptic drug
- Large doses of it can abolish ventricular tachycardia

Lidocaine

- Local anesthetic
- Used in the treatment of ventricular arrhythmia

3) Class Ic

- It is the most recent antiarrhythmic drug class
- Firstly introduced in USA in 1986
- They are the most potent as they have high affinity to Na^+ channels
- **Examples: Flecainide - Encainide - Propafenone**

